CLAIMS

What is claimed is:

1. A method of diagnosing a bone-related disorder in a human patient, the method selected from the group consisting of

a) determining the nucleotide sequence of a portion of an mrr gene of the patient and

comparing i) the nucleotide sequence of the portion and

ii) the corresponding portion of the mrr gene listed in GenBank Accession No. AF003625,

wherein a difference between

i) the nucleotide sequence of the portion and

ii) the corresponding portion of GenBank Accession No. AF003625

is an indication that the patient is afflicted with the bone-related disorder;

b) determining the nucleotide sequence of a portion of a transcript polynucleotide of a tissue of the patient, wherein the transcript polynucleotide corresponds to an mrr gene of the patient and

comparing i) the nucleotide sequence of the portion and

ii) the corresponding portion of SEQ ID NO: 2,

wherein a difference between

i) the nucleotide sequence of the portion and

ii) the corresponding portion of SEQ ID NO: 2

is an indication that the patient is afflicted with the bone-related disorder;

c) determining the amino acid sequence of a portion of an MRR protein of a tissue of the patient and

comparing i) the amino acid sequence of the portion of the MRR protein of the tissue of the patient and

ii) the corresponding portion of SEQ ID NO: 1,

wherein a difference between

i) the amino acid sequence of the portion of the MRR protein of the tissue of the patient and

ii) the corresponding portion of SEQ ID NO: 1

is an indication that the patient is afflicted with the bone-related disorder;

d) determining the level of expression of an mrr gene in a tissue of the patient and

comparing i) the level of expression of the mrr gene in the tissue of the patient and

ii) the level of expression of the mrr gene in the same tissue of a human not afflicted with the bone-related disorder,

wherein a difference between

i) the level of expression of the mrr gene in the tissue of the patient and

ii) the level of expression of the mrr gene in the same tissue of the human not afflicted with the bone-related disorder

is an indication that the patient is afflicted with the bone-related disorder;

e) determining the MRR protein content of a tissue of the patient and

comparing i) the MRR protein content of the tissue of the patient and

ii) the MRR protein content of the same tissue of a human not afflicted with the bone-related disorder,

wherein a difference between

i) the MRR protein content of the tissue of the patient and

ii) the MRR protein content of the same tissue of the human not afflicted with the bone-related disorder

is an indication that the patient is afflicted with the bone-related disorder;

f) administering a detectable MRR-binding agent to the patient,

detecting the amount of the MRR-binding agent in the patient,

and

comparing i) the amount of the MRR-binding agent in the patient and

ii) the amount of the MRR-binding agent in a human not afflicted with the bone-related disorder following administration of the MRR-binding agent thereto,

wherein a difference between

i) the amount of the MRR-binding agent in the patient and

ii) the amount of the MRR-binding agent in the human not afflicted with the bone-related disorder following administration of the MRR-binding agent thereto

is an indication that the patient is afflicted with the bone-related disorder;

and

g) administering a detectable MRR-binding agent to the patient,

detecting the amount of the MRR-binding agent associated with a bone tissue in the patient,

and

comparing i) the amount of the MRR-binding agent associated with a bone tissue in the patient and

ii) the amount of the MRR-binding agent associated with a bone tissue in a human not afflicted with the bone-related disorder following administration of the MRR-binding agent thereto,

wherein a difference between

i) the amount of the MRR-binding agent associated with a bone tissue in the patient and

ii) the amount of the MRR-binding agent associated with a bone tissue in the human not afflicted with the bone-related disorder following administration of the MRR-binding agent thereto

is an indication that the patient is afflicted with the bone-related disorder.

2. The method of claim 1, wherein the bone-related disorder is selected from the group consisting of osteoporosis, Paget's disease, hyperthyroidism, hyperparathyroidism, osteomalacia, chronic renal failure, Cushing's syndrome, an osteogenic cancer, and a non-osteogenic cancer that has metastasized to bone tissue.

3. The method of claim 1, wherein the tissue of the patient is a bone tissue.

4. The method of claim 1, wherein the tissue of the patient is tissue sample obtained from the patient.

5. The method of claim 4, wherein the tissue sample is selected from the group consisting of a bone tissue biopsy, a blood fluid, and a cerebrospinal fluid.

6. The method of claim 1, wherein the human not afflicted with the bone-related disorder is a consensus profile of humans not afflicted with the bone-related disorder.

7. The method of claim 1, wherein the transcript polynucleotide is an mRNA.

8. The method of claim 1, wherein the transcript polynucleotide is a cDNA.

9. The method of claim 8, wherein the portion of the cDNA is the entire open reading frame corresponding to the cDNA

10. The method of claim 1, wherein the MRR-binding agent is an antibody substance.

11. The method of claim 10, wherein the antibody substance is attached to an imaging agent.

12. The method of claim 11, wherein the amount of the MRR-binding agent is detected using an imaging method in which the imaging agent can be detected.

13. The method of claim 1, wherein the mrr gene listed in GenBank Accession No. AF003625 includes nucleotide residues 27599 through 32411 of GenBank Accession No. AF003625.

14. The method of claim 1, wherein the portion of the MRR protein is the entire amino acid sequence of the MRR protein.

15. A method of determining whether an individual is predisposed to become afflicted with a bone-related disorder, the method selected from the group consisting of

a) determining the nucleotide sequence of a portion of an mrr gene of the patient and

comparing i) the nucleotide sequence of the portion and

ii) the corresponding portion of the mrr gene listed in GenBank Accession No. AF003625,

wherein a difference between

i) the nucleotide sequence of the portion and

ii) the corresponding portion of GenBank Accession No. AF003625

is an indication that the patient is predisposed to become afflicted with the bone-related disorder;

b) determining the nucleotide sequence of a portion of a transcript polynucleotide of a tissue of the patient, wherein the transcript polynucleotide corresponds to an mrr gene of the patient and

comparing i) the nucleotide sequence of the portion and

ii) the corresponding portion of SEQ ID NO: 2,

wherein a difference between

i) the nucleotide sequence of the portion and

ii) the corresponding portion of SEQ ID NO: 2

is an indication that the patient is predisposed to become afflicted with the bone-related disorder;

and

c) determining the amino acid sequence of a portion of an MRR protein of a tissue of the patient and

comparing i) the amino acid sequence of the portion of the MRR protein of the tissue of the patient and

ii) the corresponding portion of SEQ ID NO: 1,

wherein a difference between

i) the amino acid sequence of the portion of the MRR protein of the tissue of the patient and

ii) the corresponding portion of SEQ ID NO: 1

is an indication that the patient is predisposed to become afflicted with the bone-related disorder.

16. The method of claim 15, wherein the bone-related disorder is selected from the group consisting of osteoporosis, Paget's disease, hyperthyroidism, hyperparathyroidism, osteomalacia, chronic renal failure, Cushing's syndrome, an osteogenic cancer, and a non-osteogenic cancer that has metastasized to bone tissue.

17. A method of alleviating a bone-related disorder in a human patient, the method selected from the group consisting of:

a) providing a biologically active portion of an MRR protein to a bone tissue of the patient in an amount sufficient to alleviate the bone-related disorder;

b) providing a non-functional MRR protein to a bone tissue of the patient in an amount sufficient to alleviate the bone-related disorder;

c) providing an expression vector comprising a polynucleotide encoding a biologically active portion of an MRR protein to a bone tissue of the patient in an amount sufficient to alleviate the bone-related disorder;

d) providing an expression vector comprising a polynucleotide encoding a non-functional MRR protein to a bone tissue of the patient in an amount sufficient to alleviate the bone-related disorder;

e) providing an agonist of MRR protein activity to a bone tissue of the patient in an amount sufficient to alleviate the bone-related disorder;

f) providing an antagonist of MRR protein activity to a bone tissue of the patient in an amount sufficient to alleviate the bone-related disorder;

g) providing an enhancer of mrr expression to a bone tissue of the patient in an amount sufficient to alleviate the bone-related disorder;

and

h) providing an inhibitor of mrr expression to a bone tissue of the patient in an amount sufficient to alleviate the bone-related disorder.

18. The method of claim 17, wherein the bone-related disorder is selected from the group consisting of osteoporosis, Paget's disease, hyperthyroidism, hyperparathyroidism, osteomalacia, chronic renal failure, Cushing's syndrome, an osteogenic cancer, and a non-osteogenic cancer that has metastasized to bone tissue.

19. The method of claim 17, wherein the biologically active portion of the MRR protein is a protein having the sequence SEQ ID NO: 1.

20. The method of claim 17, wherein the polynucleotide encoding a biologically active portion of an MRR protein is a polynucleotide having the sequence SEQ ID NO: 2.

21. The method of claim 17, wherein the antagonist of MRR protein activity is an antibody substance which binds specifically with MRR protein.

22. The method of claim 17, wherein the inhibitor of mrr expression is selected from the group consisting of an anti-sense oligonucleotide and a ribozyme.

23. A method of inhibiting a bone-related disorder in a human patient at risk for developing the bone-related disorder, the method selected from the group consisting of:

a) providing a biologically active portion of an MRR protein to a bone tissue of the patient in an amount sufficient to inhibit the bone-related disorder;

b) providing a non-functional MRR protein to a bone tissue of the patient in an amount sufficient to inhibit the bone-related disorder;

c) providing an expression vector comprising a polynucleotide encoding a biologically active portion of an MRR protein to a bone tissue of the patient in an amount sufficient to inhibit the bone-related disorder;

d) providing an expression vector comprising a polynucleotide encoding a non-functional MRR protein to a bone tissue of the patient in an amount sufficient to inhibit the bone-related disorder;

e) providing an agonist of MRR protein activity to a bone tissue of the patient in an amount sufficient to inhibit the bone-related disorder;

f) providing an antagonist of MRR protein activity to a bone tissue of the patient in an amount sufficient to inhibit the bone-related disorder;

g) providing an enhancer of mrr expression to a bone tissue of the patient in an amount sufficient to inhibit the bone-related disorder;
and

h) providing an inhibitor of mrr expression to a bone tissue of the patient in an amount sufficient to inhibit the bone-related disorder.

24. The method of claim 23, wherein the bone-related disorder is selected from the group consisting of osteoporosis, Paget's disease, hyperthyroidism, hyperparathyroidism, osteomalacia, chronic renal failure, Cushing's syndrome, an osteogenic cancer, and a non-osteogenic cancer that has metastasized to bone tissue.

25. A method of determining whether a test composition is useful for alleviating a bone-related disorder, the method selected from the group consisting of:

a) maintaining a cell which comprises a biologically active MRR protein in the presence of the test composition and

comparing i) an activity of the MRR protein of the cell maintained in the presence of the test composition and

ii) the same activity of the MRR protein of a cell of the same type maintained in the absence of the test composition,

wherein a difference between

i) an activity of the MRR protein of the cell maintained in the presence of the test composition and

ii) the same activity of the MRR protein of the cell of the same type maintained in the absence of the test composition

is an indication that the test composition is useful for alleviating a bone-related disorder;

b) maintaining a cell which comprises a biologically active MRR protein in the presence of the test composition and

comparing i) the level of expression of the mrr gene in the cell maintained in the presence of the test composition and

ii) the level of expression of the mrr gene in the MRR protein of a cell of the same type maintained in the absence of the test composition,

wherein a difference between

i) the level of expression of the mrr gene in the cell maintained in the presence of the test composition and

ii) the level of expression of the mrr gene in the MRR protein of a cell of the same type maintained in the absence of the test composition

is an indication that the test composition is useful for alleviating a bone-related disorder;

c) maintaining a cell which comprises a biologically active MRR protein in the presence of the test composition and

comparing i) a bone phenotype of the cell maintained in the presence of the test composition and

ii) the same bone phenotype of a cell of the same type maintained in the absence of the test composition,

wherein a difference between

i) the bone phenotype of the cell maintained in the presence of the test composition and

ii) the same bone phenotype of the cell maintained in the absence of the test composition

is an indication that the test composition is useful for alleviating a bone-related disorder;

d) administering the test composition to a first animal which naturally harbors an mrr gene and

comparing i) a bone phenotype of the first transgenic animal and

ii) the same bone phenotype of a second animal which naturally harbors an mrr gene and to which the test composition is not administered,

wherein a difference between

i) the bone phenotype of the first animal and

ii) the same bone phenotype of the second animal

is an indication that the test composition is useful for alleviating a bone-related disorder;

e) administering the test composition to a first non-human transgenic animal which harbors an exogenous mrr gene and

comparing i) a bone phenotype of the first transgenic animal and

ii) the same bone phenotype of a second non-human transgenic animal which harbors an exogenous mrr gene and to which the test composition is not administered,

wherein a difference between

i) the bone phenotype of the first transgenic animal and

ii) the same bone phenotype of the second transgenic animal

is an indication that the test composition is useful for alleviating a bone-related disorder; and

f) maintaining an artificial membrane which comprises a biologically active MRR protein in the presence of the test composition and

comparing i) an activity of the MRR protein of the artificial membrane maintained in the presence of the test composition and

ii) the same activity of the MRR protein of an artificial membrane of the same type maintained in the absence of the test composition,

wherein a difference between

i) the activity of the MRR protein of the artificial membrane maintained in the presence of the test composition and

ii) the same activity of the MRR protein of artificial membrane of the same type maintained in the absence of the test composition

is an indication that the test composition is useful for alleviating a bone-related disorder.

26. The method of claim 25, wherein the bone-related disorder is selected from the group consisting of osteoporosis, Paget's disease, hyperthyroidism, hyperparathyroidism, osteomalacia, chronic renal failure, Cushing's syndrome, an osteogenic cancer, and a non-osteogenic cancer that has metastasized to bone tissue.

27. The method of claim 25, wherein the biologically active MRR protein is a protein having the amino acid sequence SEQ ID NO: 1.

28. The method of claim 25, wherein the activity of the MRR protein is selected from the group consisting of a proteolytic activity, a pore-modulating activity, an enzyme-modulating activity, and a gene transcription-modulating activity.

29. The method of claim 25, wherein the cell is an animal cell.

30. The method of claim 29, wherein the cell is a bone cell.

31. The method of claim 30, wherein the animal cell is selected from the group consisting of a human cell, a mouse cell, and a rat cell.

32. The method of claim 25, wherein the mrr gene is selected from the group consisting of a human mrr gene, a mouse mrr gene, and a rat mrr gene.

33. The method of claim 32, wherein the mrr gene encodes a protein having an amino acid sequence selected from the group consisting of SEQ ID NOs: 1 and 3.

34. The method of claim 25, wherein the bone phenotype is selected from the group consisting of a bone deposition phenotype, a bone resorption phenotype, and a bone morphology phenotype.

35. The method of claim 25, wherein the exogenous mrr gene encodes a protein having the amino acid sequence SEQ ID NO: 1.

36. The method of claim 25, wherein the artificial membrane is selected from the group consisting of a liposome and a re-sealed erythrocyte.

37. A method of determining the propensity of a test compound to induce a bone-related disorder in a human patient, the method selected from the group consisting of:

a) maintaining a cell which comprises a biologically active MRR protein in the presence of the test composition and

comparing i) an activity of the MRR protein of the cell maintained in the presence of the test composition and

ii) the same activity of the MRR protein of a cell of the same type maintained in the absence of the test composition,

wherein a difference between

i) an activity of the MRR protein of the cell maintained in the presence of the test composition and

ii) the same activity of the MRR protein of the cell of the same type maintained in the absence of the test composition

is an indication that the test composition is likely to induce the bone-related disorder in a human patient;

b) maintaining a cell which comprises a biologically active MRR protein in the presence of the test composition and

comparing i) the level of expression of the mrr gene in the cell maintained in the presence of the test composition and

ii) the level of expression of the mrr gene in the MRR protein of a cell of the same type maintained in the absence of the test composition,

wherein a difference between

i) the level of expression of the mrr gene in the cell maintained in the presence of the test composition and

ii) the level of expression of the mrr gene in the MRR protein of a cell of the same type maintained in the absence of the test composition

is an indication that the test composition is likely to induce the bone-related disorder in a human patient;

c) maintaining a cell which comprises a biologically active MRR protein in the presence of the test composition and

comparing i) a bone phenotype of the cell maintained in the presence of the test composition and

ii) the same bone phenotype of a cell of the same type maintained in the absence of the test composition,

wherein a difference between

i) the bone phenotype of the cell maintained in the presence of the test composition and

ii) the same bone phenotype of the cell maintained in the absence of the test composition

is an indication that the test composition is likely to induce the bone-related disorder in a human patient;

d) administering the test composition to a first animal which naturally harbors an mrr gene and

comparing i) a bone phenotype of the first transgenic animal and

ii) the same bone phenotype of a second animal which naturally harbors an mrr gene and to which the test composition is not administered,

wherein a difference between

i) the bone phenotype of the first animal and

ii) the same bone phenotype of the second animal

is an indication that the test composition is likely to induce the bone-related disorder in a human patient;

e) administering the test composition to a first non-human transgenic animal which harbors an exogenous mrr gene and

comparing i) a bone phenotype of the first transgenic animal and

ii) the same bone phenotype of a second non-human transgenic animal which harbors an exogenous mrr gene and to which the test composition is not administered,

wherein a difference between

i) the bone phenotype of the first transgenic animal and

ii) the same bone phenotype of the second transgenic animal

is an indication that the test composition is likely to induce the bone-related disorder in a human patient;

and

f) maintaining an artificial membrane which comprises a biologically active MRR protein in the presence of the test composition and

comparing i) an activity of the MRR protein of the artificial membrane maintained in the presence of the test composition and

ii) the same activity of the MRR protein of an artificial membrane of the same type maintained in the absence of the test composition,

wherein a difference between

i) an activity of the MRR protein of the artificial membrane maintained in the presence of the test composition and

ii) the same activity of the MRR protein of artificial membrane of the same type maintained in the absence of the test composition

is an indication that the test composition is likely to induce the bone-related disorder in a human patient.

38. The method of claim 37, wherein the bone-related disorder is selected from the group consisting of osteoporosis, Paget's disease, hyperthyroidism, hyperparathyroidism, osteomalacia, chronic renal failure, Cushing's syndrome, an osteogenic cancer, and a non-osteogenic cancer that has metastasized to bone tissue.

39. A method of identifying a polymorphism associated with an mrr gene of a human patient afflicted with a bone-related disorder, the method comprising

determining the nucleotide sequence of a polynucleotide associated with the mrr gene in the patient and

comparing i) the nucleotide sequence of a polynucleotide associated with the mrr gene in the patient and

ii) the nucleotide sequence of the corresponding portion of an mrr gene of a human not afflicted with the bone-related disorder,

wherein a difference between

i) the nucleotide sequence of the polynucleotide and

ii) the nucleotide sequence of the corresponding portion of an mrr gene of the human not afflicted with the bone-related disorder

indicates a polymorphism associated with the mrr gene of the human patient afflicted with the bone-related disorder.

40. The method of claim 39, wherein the bone-related disorder is selected from the group consisting of osteoporosis, Paget's disease, hyperthyroidism, hyperparathyroidism, osteomalacia, chronic renal failure, Cushing's syndrome, an osteogenic cancer, and a non-osteogenic cancer that has metastasized to bone tissue.

41. A method of determining whether a human patient is predisposed to become afflicted with a bone-related disorder, the method comprising determining whether a polymorphism identified by the method of claim 39 occurs in an mrr gene of the human patient, wherein occurrence of the polymorphism in the mrr gene of the human patient is an indication that the human patient is predisposed to become afflicted with the bone-related disorder.